RO219-SD-WEB3

# Hafnium Oxide Nanoparticles Activated by Radiotherapy Induce an Anti-Tumor Immune Response

Wednesday, Dec. 4 12:45PM - 1:15PM Room: RO Community, Learning Center Station #3

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## PURPOSE

First in class hafnium oxide nanoparticles (NBTXR3) activated by radiotherapy (RT) increase radiation dose deposit within cancer cells compared to RT alone. Given that RT can prime an anti-tumor immune response we hypothesized that this response could be enhanced by NBTXR3+RT in both animals and humans.

## METHOD AND MATERIALS

Different abscopal assays in mice were conducted. Immunocompetent mice were injected in both flanks with murine tumor cells. Intratumoral injection of NBTXR3 (or vehicle) was performed in right flank tumors, followed by RT of right flank tumors only. Tumor growth was followed and immune cell infiltrates were analyzed by immunohistochemistry (IHC). Some mice received anti-PD-1 injections and tumor growth was monitored. Pts with locally advanced soft tissue sarcoma (STS) [NCT02379845] received either NBTXR3+RT or RT alone. Pts pre- and post-treatment tumor tissues were analyzed by IHC and Digital Pathology for immune biomarkers.

## RESULTS

Animal studies demonstrated that NBTXR3+RT induces an immune response which was not observed with RT alone. IHC showed significantly more CD8+ cells present in NBTXR3+RT treated and untreated tumors. Furthermore, NBTXR3+RT improved the effect of anti-PD-1. Similarly, increased CD8+ T cell infiltration pre- vs post-treatment was observed in tumor tissues from STS pts treated with NBTXR3+RT. An increase in biomarkers, including CD8, following NBTXR3+RT was also observed by IHC in tumor samples from STS pts compared to RT alone.

## CONCLUSION

These results demonstrate that NBTXR3+RT induces a specific adaptive immune profile in both mice and

STS pts. NBTXR3+RT also improved response to anti-PD-1 in mice, opening the potential for combination with immunotherapeutic agents in humans. We have therefore sought to investigate the safety and systemic effect of NBTXR3 activated by stereotactic ablative radiotherapy (SABR) in combination with anti-PD-1 in pts with locoregionally recurrent or metastatic (lung or liver) head and neck squamous cell carcinoma, as well as in metastatic non-small cell lung cancer and liver metastasis pts [NCT03589339].

## CLINICAL RELEVANCE/APPLICATION

The results of this study highlight the potential of NBTXR3 to be used in combination with immune checkpoint inhibitors in order to improve patient outcomes.

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